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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,967	GLOMBIK ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 4 and 6 are objected to because of the following informalities: Claims 4 and 6 recite abbreviations for some active ingredients. The expansion for these abbreviations with the abbreviation within parentheses should be recited in the first occurrence of each abbreviation.

In Claim 4, the term "lipase inhibitor" appears twice.

Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities:

At page 4, the names of amino acids listed should be aligned properly.

The heading 'Table 1' should be moved from page 9 to the top of page 10 if the structures appearing on page 10 are the contents of Table 1.

Blank sections appear at page 10 and 17.

In the examples at page 14 and 15 the entries do not appear to be aligned properly.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 recite the term C_0 alkyl. It is not clear what applicants intend by this term since an alkyl by definition must have at least one carbon.

Claim 1 recites the term derivative. In the absence of the specific derivatizations to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of the derivatives of this invention, the identity of said derivatives would be difficult to describe and the metes and bounds of the said derivatives applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated.

In Claim 4 it is not clear if the "a" within parentheses in lipoprotein (a) is a limitation. If it is a limitation the parentheses should be removed. The claim also recites "lipase/amylase inhibitor". It is not clear if it is a single inhibitor or two inhibitors in combination or either one of these two.

The term "normalizes" in claims 5 and 6 is a relative term that renders the claims indefinite. The term "normalizes" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the

explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation cholesterol absorption inhibitors, and the claim also recites ezetimibe, tiqueside and parmequeside, which is the narrower statement of the range/limitation.

Claim 9 contains the trademark/trade name Caromax. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an active ingredient in the instant composition and, accordingly, the identification/description is indefinite.

Claims 11, 13, 15 and 20 recite a pharmaceutically effective amount or a subclinical pharmaceutically effective amount of the compound of formula I and another active ingredient such that the combination results in the amount of the composition of matter being

pharmaceutically effective. It is not clear what is meant by subclinical pharmaceutically effective amount. If a pharmaceutically effective amount of instant compound of formula I and a pharmaceutically effective amount of the other active ingredient is combined then the resulting combination should give a composition that is also pharmaceutically effective. It is not clear what is being claimed since the claim language makes the overall claim look obvious. The claim is being interpreted as the said composition of matter comprising a pharmaceutically amount of each of the two active ingredients.

Claim 16 recites a physiological condition. In the absence of a specific condition for the said prophylaxis or treatment the recitation is broad and is interpreted to mean any condition.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 and 20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-6 of U.S. Patent No. 6,387,944 ('944

patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1-7 and 20 are drawn to a composition comprising a compound of formula (I) and at least one other active ingredient or pharmaceutically acceptable salts or physiologically functional derivatives with the at least one other active ingredient being a compound HMG-CoA reductase inhibitor or cholesterol absorption inhibitor or a compound that normalizes lipid metabolism wherein the specific lipid metabolism normalizer can be statins and a composition comprising effective amounts of both the active ingredients.

These limitations are also seen in claims 5 and 6 of the '944 patent that comprise compounds that are recited in formula (I) of instant claim 1. The other active ingredient in claim 6 of the '944 patent is statin.

It would be obvious to one of ordinary skill in the art that the composition of the instant claims and the compositions of the claims in the '944 patent are substantially overlapping. The compositions of the instant application should recite limitations that are patentably distinct over those of the '944 patent.

Claims 1-7 and 20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-20 of U.S. Patent No. 6,221,897 ('897 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1-7 and 20 are drawn to a composition comprising a compound of formula (I) and at least one other active ingredient or pharmaceutically acceptable salts or physiologically

functional derivatives with the at least one other active ingredient being a compound HMG-CoA reductase inhibitor or cholesterol absorption inhibitor or a compound that normalizes lipid metabolism wherein the specific lipid metabolism normalizer can be statins and a composition comprising effective amounts of both the active ingredients.

These limitations are also seen in claims 19 and 20 of the '897 patent that comprise compounds that are recited in formula (I) of instant claim 1. The other active ingredient in claim 20 of the '897 patent is statin.

It would be obvious to one of ordinary skill in the art that the composition of the instant claims and the compositions of the claims in the '897 patent are substantially overlapping. The compositions of the instant application should recite limitations that are patentably distinct over those of the '897 patent.

Claims 1-7 and 20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,441,022 ('022 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1-7 and 20 are drawn to a composition comprising a compound of formula (I) and at least one other active ingredient or pharmaceutically acceptable salts or physiologically functional derivatives with the at least one other active ingredient being a compound HMG-CoA reductase inhibitor or cholesterol absorption inhibitor or a compound that normalizes lipid metabolism wherein the specific lipid metabolism normalizer can be statins and a composition comprising effective amounts of both the active ingredients.

These limitations are also seen in claims 1-8 of the '022 patent that comprise compounds that are recited in formula (I) of instant claim 1 and also include various statins that are active ingredients.

It would be obvious to one of ordinary skill in the art that the composition of the instant claims and the compositions of the claims in the '022 patent are substantially overlapping. The compositions of the instant application should recite limitations that are patentably distinct over those of the '022 patent.

Claims 1-7 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-35 of copending Application No. 10/606,771 ('771 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1-7 and 20 are drawn to a composition comprising a compound of formula (I) and at least one other active ingredient or pharmaceutically acceptable salts or physiologically functional derivatives with the at least one other active ingredient being a compound HMG-CoA reductase inhibitor or cholesterol absorption inhibitor or a compound that normalizes lipid metabolism wherein the specific lipid metabolism normalizer can be statins and a composition comprising effective amounts of both the active ingredients.

Claims 31-40 of the copending '771 application are also drawn to a composition comprising compounds of formula (I) that has a coating. The additional recitation "coating" is not seen to be a patentable distinction. There is substantial overlap between instant claims 1-7 and 20 and claims 31-40 of the copending '771 application.

The instant claims should recite limitations that are patentably distinct over those of the copending '771 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Joint Inventors

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 and 21 are rejected under 35 U.S.C. 103(a) as being obvious over Frick et al (US 6221897) in combination with AHFS Drug Information 1994, pages 1096-1102.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Fricke et al disclose composition comprising benzothiepine 1,1-dioxide derivatives of formula I in which R^1 is butyl, ethyl; R^2 is OH; R^3 is a saccharide residue; R^4 and R^5 are methyl and Z is –(C=O)-C0-C6-alkyl-NH- (see col. 23, lines 1-67; col. 25, line 57 through col. 26, line 2). The composition disclosed by Fricke et al has other pharmaceutically active compounds including, in particular, one or more statins as another active ingredient (see col. 3, lines 1-18 and 45-47). The compositions are made by uniform and homogeneous mixing of the active

compound with a liquid and/or finely divided solid excipient and additional constituents (see col. 4, lines 9-20).

One of the statins for example lovastatin is an HMG-CoA inhibitor, a cholesterol absorption inhibitor and also antilipemic agent, with a dosage of about 20-80 mg/day and with no apparent toxic effects (see AHFS Drug Information 1994, pages 1096-1102).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and another active agent to make a composition comprising both the active ingredients in individually effective amounts such that the combination results in an amount of the composition that is also pharmaceutically effective, since the both the active ingredients and their effective dosage is seen to be taught individually in the prior art of record.

It is obvious to combine individual compounds taught to have the same utility to form a new composition comprising the two for the very same purpose (In re Kerkhoven, 626 F. 2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980)).

Claims 1-3, 6-8 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Frick et al (US 6221897) in combination with Castaner (Drugs of the Future, 2000, 25(7), 679-685).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 are drawn to a composition of matter comprising a compound of formula (I) and another active ingredient. Dependent claims 7, 8 and 20 recite limitations wherein the other active ingredient is a cholesterol absorption inhibitor, specific cholesterol absorption inhibitors and a pharmaceutically effective amount of the compound of formula (I) and the other active ingredient.

Fricke et al disclose composition comprising benzothiepine 1,1-dioxide derivatives of formula I in which R^1 is butyl, ethyl; R^2 is OH; R^3 is a saccharide residue; R^4 and R^5 are methyl and Z is –(C=O)-C0-C6-alkyl-NH- (see col. 23, lines 1-67; col. 25, line 57 through col. 26, line 2). The compound of formula (I) and their pharmaceutically tolerable salts and physiologically functional derivatives are ideal pharmaceuticals for treating hyperlipidemia and also lowering serum cholesterol level (col. 3, lines 1-13). The composition disclosed by Fricke et al has other pharmaceutically active compounds as another active ingredient (see col. 3, lines 1-18 and 45-47). Fricke also teaches effective dosage amounts of the compounds of formula (I) (col. 3, lines 20-30).

However, Fricke et al do not teach a composition comprising the compound of formula (I) and a cholesterol absorption inhibitor chosen from ezetimibe, tiqueside or pamaqueside as the other active ingredient.

Castaner, drawn to hypolipidemic cholesterol absorption inhibitor, teach that ezetimibe is a potent cholesterol absorption inhibitor. It is very potent in inhibiting increases in plasma cholesterol (page 682, right column, line 10 through page 683, left column, line 13; page 684, right column, see paragraph starting under subtitle-Clinical Studies).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and another active agent like ezetimibe to make a third composition comprising both the active ingredients in individually effective amounts such that the combination results in an amount of the composition that is also pharmaceutically effective, since the both the active ingredients and their effective dosage is seen to be taught individually in the prior art of record.

It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose (In re Kerkhoven, 626 F. 2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980)).

Claims 10-19 are rejected under 35 U.S.C. 103(a) as being obvious over Frick et al (US 6221897) in combination with AHFS Drug Information 1994, pages 1096-1102.

Claims 10-19 are drawn to a method for effecting the prophylaxis and treatment of a lipid metabolism disorder or metabolic syndrome, hyperlipidemia, arteriosclerotic manifestations, a physiological condition comprising administering a pharmaceutically effective amount of the composition comprising the compound of formula (I) and another active ingredient and the method wherein a pharmaceutically effective amount or a subclinical pharmaceutically effective amount of the compound of formula I and another active ingredient such that the combination results in the amount of the composition of matter being pharmaceutically effective.

Fricke et al disclose benzothiepine 1,1-dioxide derivatives of formula I in which R^1 is butyl, ethyl; R^2 is OH; R^3 is a saccharide residue; R^4 and R^5 are methyl and Z is –(C=O)-C0-C6-alkyl-NH- and compositions comprising these compounds (see col. 25-26, claims 19 and 20).

The composition disclosed by Fricke et al has other pharmaceutically active compounds including one or more statins as another active ingredient (see col. 3, lines 1-50). One of the statins for example lovastatin is an HMG-CoA inhibitor, a cholesterol absorption inhibitor and an antilipemic agent with a dosage of about 20-80 mg/day with no apparent toxic effects (see AHFS Drug Information 1994, pages 1096-1102).

Fricke et al also teach the use of compounds of formula (I) and their derivatives in a method for the prophylaxis or treatment of hyperlipidemia, arteriosclerotic symptoms, lipid metabolism disorder and arteriosclerotic symptoms (see cols. 23-26). They also state that for the prophylaxis or therapy of these conditions the compounds of formula I of their invention can optionally also be administered in combination with active agents like statins (see col. 3, lines 5-47). Also, according to their disclosure one of ordinary skill in the art has many means to determine or predict the needs of the patient for such prophylaxis and therapy and that these methods are well known in the art. According to this disclosure then, one of ordinary skill in the art can determine the time of administration in addition to other factors (see col. 3., lines12-15), including the dosage as taught by Fricke (col. 3, lines 21-40). Hence it is well within the purview of one of ordinary skill in the art to combine the effective amounts of the compound of formula (I) and the effective amount of the other active ingredient to obtain a composition that is pharmaceutically effective.

It would have been obvious to one of ordinary skill in the at the time the invention was made to use the composition as instantly claimed in a method for the treatment or prophylaxis of the said disorder or conditions or manifestations with reasonable amount of success since the same is seen to be taught in the prior art cited.

One of ordinary skill in the art would be motivated to do so since the compounds of Fricke are more active by a factor of 20 to 100 compared with compounds previously known (see col. 8, lines 29-32) and have improved availability (see col. 1, lines 23-32) and the statins like lovastatin also reach peak plasma concentrations within 2-6 hours. Hence it would be logical to use a composition comprising both these active compounds in a method for the prophylaxis or treatment of the disorders as instantly claimed.

Conclusion

Claims 1-21 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK

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